

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Part 334**

[Docket No. 78N-036L]

**Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph**

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice of proposed rulemaking.

**SUMMARY:** The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that amends the tentative final monograph for over-the-counter (OTC) laxative drug products by modifying the directions for the use of bulk laxatives. This notice is part of the ongoing review of OTC drug products conducted by FDA.

**DATES:** Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by December 1, 1986. New data relating to the directions for the use of OTC bulk laxatives by October 1, 1987. Comments on the new data by December 1, 1987. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by January 29, 1987.

**ADDRESS:** Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

**SUPPLEMENTARY INFORMATION:** In the *Federal Register* of March 21, 1975 (40 FR 12902), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC laxative, antidiarrheal, emetic, and antiemetic drug products, together with the recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. The agency's proposed regulation, in the form of a tentative final monograph, for OTC laxative drug products was published in the *Federal*

*Register* of January 15, 1985 (50 FR 2124). Interested persons were invited to file by May 15, 1985, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal.

In this amendment to the tentative final monograph, FDA is modifying its position on the directions for use and the dosage of OTC bulk laxative drug products that were proposed in Part 334 (50 FR 2124). Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC laxative drug products.

In comment 12 of the tentative final monograph (50 FR 2126), the agency stated that some of the Panel's recommendations regarding the directions for use of OTC laxative drug products required clarification. The agency stated that where the Panel recommended a daily dose of an ingredient without a dosage interval, the agency was proposing this to mean a single daily dose. However, in reviewing some of the comments submitted in response to the tentative final monograph and in further reviewing the directions for use of marketed bulk laxative drug products and the data on these products that were submitted to the Panel, the agency has found that the maximum daily dose of bulk laxatives is routinely administered in divided doses rather than as a single dose. In addition, the maximum daily dose of some bulk laxatives is so large that it may pose a risk of esophageal obstruction if taken at one time (Ref. 1). This risk can be minimized by administering bulk laxatives in divided doses rather than in a single daily dose, as originally proposed by the agency in the directions in the earlier tentative final monograph. The agency also recognizes that OTC bulk laxative ingredients are effective over a wide range of doses and dosing intervals; therefore, the dosages specified in the monograph for these drug products should be sufficiently flexible to accommodate the various dosages of marketed products that have been shown to be safe and effective.

Based on a review of the available data and information, the agency is revising the dosage and directions for the use of bulk laxatives that were previously proposed in § 334.52(d) (2), (3), (4), (5), (6), and (7) of the tentative final monograph. The dosages being proposed for children are based on the relationship of 1 dose for an adult; ½ the adult dose for children 6 to under 12 years of age; and ¼ the adult dose for children 2 to under 6 years of age. Pediatric dosages for particular

ingredients have been proposed only when there is a marketing history of these ingredients being administered to children in these age groups. For example, an ingredient without a marketed pediatric dosage for children 2 to under 6 years of age will not have a dosage for this age group in the tentative final monograph.

The agency believes that these revised dosages and directions for use provide for necessary flexibility in developing appropriate directions for the wide range of OTC bulk laxative drug products.

**Reference**

(1) Brunton, L. L., "Laxatives," in "The Pharmacological Basis of Therapeutics," 7th Ed., edited by L. S. Goodman, A. Gilman, T. W. Rall, and F. Murad, The MacMillan Publishing Co., New York, pp. 996-997, 1985.

**Testing of Category II and Category III Conditions**

Interested persons may communicate with the agency about the submission of data and information relating to the directions for the use of OTC bulk laxative ingredients by following the procedures outlined in the agency's policy statement published in the *Federal Register* of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). That policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the *Federal Register* of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC laxative drug products, is a major rule.

The agency has determined that under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Interested persons may, on or before December 1, 1986, submit to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. Written comments on the agency's economic impact determination may be submitted on or before January 29, 1987. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the Office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before October 1, 1987, may also submit in writing new data relating to the directions for the use of OTC bulk laxatives. Written comments on the new data may be submitted on or before December 1, 1987. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Data and comments submitted in response to this amendment will be

considered by the agency in establishing a final monograph. Data submitted after the closing of the administrative record on December 1, 1987 will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

#### List of Subjects in 21 CFR Part 334

OTC drugs Laxative drug products.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Administrative Procedure Act, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 334 (proposed in the **Federal Register** of January 15, 1985; 50 FR 2124) as follows:

#### **PART 334—LAXATIVE DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE**

1. The authority citation for Part 334 continues to read as follows:

**Authority:** Secs. 201(p), 502, 505, 701, 52 Stat. 1041-1042 as amended, 1050-1053 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); 5 U.S.C. 553; 21 CFR 5.11.

2. In Subpart B, § 334.52 is amended by revising paragraphs (d)(2), (d)(3), (d)(4), (d)(5), (d)(6), and (d)(7), to read as follows:

#### **§ 334.52 Labeling of bulk-forming laxative drug products.**

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(d) \* \* \*  
(2) *For products containing bran identified in § 334.10(a).* Adults and children 12 years of age and over: Oral dosage is up to 14 grams daily in divided doses of 1 to 7 grams per dose. Children 6 to under 12 years of age: Up to 7 grams daily in divided doses of 1 to 3.5 grams per dose. Children 2 to under 6 years of age: Up to 3.5 grams daily in divided doses of 1 to 1.75 grams per dose. Children under 2 years of age: Consult a doctor.

(3) *For products containing methylcellulose and sodium carboxymethylcellulose identified in § 334.10(b) (1) and (2).* Adults and

children 12 years of age and over: Oral dosage is up to 6 grams daily in divided doses of 0.45 to 3 grams per dose. Children 6 to under 12 years of age: Up to 3 grams daily in divided doses of 0.45 to 1.5 grams per dose. Children under 6 years of age: Consult a doctor.

(4) *For products containing karaya identified in § 334.10(c).* Adults and children 12 years of age and over: Oral dosage is up to 14 grams daily in divided doses of 3.5 to 7 grams per dose. Children under 12 years of age: Consult a doctor.

(5) *For products containing malt soup extract identified in § 334.10(d).* Adults and children 12 years of age and over: oral dosage is up to 64 grams daily in divided doses of 3 to 32 grams per dose. Children 6 to under 12 years of age: Up to 32 grams daily in divided doses of 3 to 16 grams per dose. Children 2 to under 6 years of age: Up to 16 grams daily in divided doses of 3 to 8 grams per dose. Children under 2 years of age: Consult a doctor.

(6) *For products containing polycarbophil identified in § 334.10(e).* Adults and children 12 years of age and over: Oral dosage is up to 4 grams daily in divided doses of 1 gram per dose. Children 6 to under 12 years of age: Up to 2 grams daily in divided doses of 0.5 grams per dose. Children 2 to under 6 years of age: Up to 1 gram daily in divided doses of 0.5 grams per dose. Children under 2 years of age: Consult a doctor.

(7) *For products containing any psyllium ingredient identified in § 334.10(f).* Adults and children 12 years of age and over: Oral dosage is up to 30 grams daily in divided doses of 2.5 to 7.5 grams per dose. Children 6 to under 12 years of age: Up to 15 grams daily in divided doses of 2.5 to 3.75 grams per dose. Children under 6 years of age: Consult a doctor.

Dated: August 9, 1986.

Frank E. Young,

Commissioner of Food and Drugs.

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